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Title: Fruit Fly, Drosophila melanogaster, as an In Vivo Tool to Study the Biological Effects of Proton Irradiation

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Abstract

The clinical superiority of proton therapy (PT) over photon therapy has recently gained recognition; however, the biological effects of PT remain poorly understood. The lack of in vivo evidence is especially important. Therefore, we aimed to validate the usefulness of Drosophila melanogaster as an alternative tool in proton radiobiology. To determine whether the comparative biological effects of protons and X rays are detectable in Drosophila, we assessed their influence on survival and mRNA expression. Postirradiation observation revealed that protons inhibited their development and reduced the overall survival rates more effectively than X rays. The relative biological effectiveness of the proton beams compared to the X rays estimated from the 50% lethal doses was 1.31. At 2 or 24 h postirradiation, mRNA expression analysis demonstrated that the expression patterns of several genes (such as DNA-repair-, apoptosis- and angiogenesis-related genes) followed different time courses depending on radiation type. Moreover, our trials suggested that the knockdown of individual genes by the GAL4/UAS system changes the radiosensitivity in a radiation type-specific manner. We confirmed this Drosophila model to be considerably useful to evaluate the findings from in vitro studies in an in vivo system. Furthermore, this model has a potential to elucidate more complex biological mechanisms underlying proton irradiation.